

Acute Generalized Exanthematous Pustulosis Resembling Toxic Epidermal Necrolysis Caused by Famotidine

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We report acute generalized exanthematous pustulosis (AGEP) resembling toxic epidermal necrolysis (TEN) caused by famotidine. This presentation has been reportedly caused by other drugs (1).

CASE REPORT

A morbidly obese 60-year-old Hispanic woman with chronic obstructive pulmonary disease, renal failure and asthma but no history of skin disease was hospitalized for a putative urinary tract infection. She had developed a red pruritic painless rash 2 days after starting famotidine. She was allergic to ampicillin and had taken dexamethasone, prozac, percocet, diltiazem, theophylline, ciprofloxacin and albuterol in the preceding month's hospitalization.

Examination revealed diffuse erythema, a positive Nikolsky's sign and erosions on her torso (Fig. 1) and fragile 2–3 mm pustules over her chin, neck and forearms (Fig. 2). Her palms, soles and mucous membranes were clear. Blood analysis revealed leucocytosis (30,600/cc²), neutrophilia (95.6%) and few eosinophils (0.3%). Liver enzymes and screening for lues (RPR) were normal. Bacterial culture of blood and urine grew no organisms. Bacterial cultures of eroded neck skin grew *Staphylococcus epidermidis*. Both frozen sections and haematoxylin and eosin biopsies revealed subcorneal blistering, devoid of necrolytic keratinocytes, acantholysis, spongiosis and organisms, findings consistent with AGEP rather than TEN, pustular psoriasis or staphylococcal scalded skin syndrome. Famotidine was discontinued, clobetasol propionate

applied and the rash resolved without sequelae in 3 days.

DISCUSSION

Numerous non-follicular pinpoint sterile pustules on an erythematous background with a rapid self-healing course, fever and peripheral blood leucocytosis characterize AGEP. AGEP with its diffuse, sometimes initially scarlatiniform, erythema, oedema, occasional mucous membrane involvement (20%) and occasional targetoid lesions and Nikolsky's sign (2) can clinically resemble TEN. Usually, its fragile pustules, lack of associated morbidity and sudden onset of fragile pustules typically arising within 5 days (2.5 days when due to antibiotics) of medication intake facilitate its diagnosis.

AGEP, like many dermatological conditions, is an immunologically mediated reactive process. Drugs, viral infections (e.g. enteroviruses), mercury and ultraviolet radiation trigger AGEP. Interestingly, famotidine has been linked primarily to other acutely triggered dermatosis, specifically: leucocytoclastic vasculitis (3) erythema multiforme (4) and TEN (5). TEN and AGEP have distinct aetiologies. Whereas TEN has been linked to activation of CD-95 (FAS) and apoptosis, which accounts for its necrotic keratinocytes and response to intravenous immunoglobulin (6), AGEP has been linked to elevated IL-8 in keratinocytes and infiltrating mononuclear cells and drug-specific T-cells (7).

The particular reactive dermatosis that a stimulus elicits, eludes easy explanation but probably is based on each individual's unique T-cell population. Differing



Fig. 1. Diffuse erythema, a positive Nikolsky's sign and erosions on the torso.

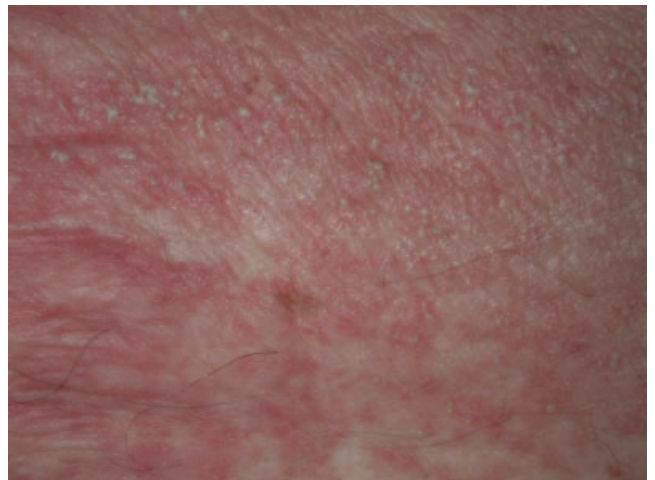


Fig. 2. Fragile 2–3 mm pustules over the chin, neck and forearms.

stimuli, durations of stimuli and T-cell subsets might also account for manifestations of AGEP that include leucocytoclastic vasculitis (8), massive lymphadenopathy (9) and widespread erosions that mimic TEN (10). Recognition that AGEP can resemble TEN, a distinction that can be made with a fresh frozen section, if diagnostic confusion exists, is important so that AGEP, which resolves if the offending agent is discontinued, is not over treated.

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